

REVIEW ARTICLE

Extended Lymph Node Dissection in Gastrointestinal Cancer

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We reviewed the literature concerning the effect of extended lymph node dissection on survival in patients with gastrointestinal cancer. Most retrospective and/or prospective nonrandomized comparative studies have claimed that extended lymph node dissection significantly improves survival rate in patients with esophageal cancer, gastric cancer, and colorectal cancer. However, it is difficult to interpret these results since specialized care provided in trials may itself improve survival. In gastric cancer, several prospective randomized trials have failed to demonstrate a survival advantage of extended dissection, while there are few well-done prospective randomized trials in esophageal or colorectal cancer. Therefore, the therapeutic value of extended lymph node dissection remains to be determined in gastrointestinal cancer. Randomized prospective studies within the bounds of the ethical treatment of patients can and should be done.

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KEY WORDS: lymph node dissection; esophageal cancer; gastric cancer; colorectal cancer

INTRODUCTION

Traditionally, trapping of tumor cells in regional lymph nodes has been assumed to be critical in the prevention of systemic spread of malignant cells from a primary cancer. Curative surgery comprises en bloc resection of the primary tumor together with the regional lymph nodes. This surgical approach was initiated by Halsted [1] for the cure of breast carcinoma about 100 years ago, and it has been generally accepted as the appropriate surgical treatment for gastrointestinal cancer. In gastrointestinal cancer, chemotherapy is of limited therapeutic value, and surgery offers the only hope for cure. Lymph node dissection has been performed, assuming that the best chance for cure is achieved when the highest dissected lymph node is free of tumor. However, laboratory studies indicate that lymph node "filtration" of tumor cells may be incomplete or ineffective [2], and that many lymphatic and lymphaticovenous shunts bypass regional lymph nodes, allowing both lymphatic and hema-

togenous dissemination of malignant cells [3-5]. There is also evidence that lymphatic and hematogenous dissemination occurs not in serial, but in parallel patterns [6,7]. These points emphasize that regional lymph node metastases are indicators, but do not govern survival in cancer [6]. Indeed, in breast cancer a number of prospective randomized trials have demonstrated that axillary or internal mammary lymph node dissection in conjunction with mastectomy does not alter the incidence of systemic recurrence or patient survival [8-10], although axillary lymph node dissection remains a reliable method of assessing nodal status and providing regional control [11,12].

There are few well-conducted prospective randomized trials that directly address the issue of lymph node con-

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TABLE I. Retrospective Studies Comparing Conventional Vs. Extended Esophagectomy in Patients With Esophageal Cancer

Authors/ type of resection	No. of patients	Outcome	
Skinner et al. [26]		<u>Overall survival rate at 18 months</u>	
Standard resection	21	14%] $p < .005$
En bloc resection	31	55%	
		5-year survival rate	
Lerut et al. [28]		<u>Stages III and IV</u>	<u>Overall</u>
Curative nonradical	75	13%] $p = .002$
Curative radical	54	22%	

trol of cancer cell dissemination in gastrointestinal cancer. Many surgeons adopt lymph node dissection for these cancer operations on the basis of their experience and outcomes of reported cases [13]. The discrepancy between the surgical management of breast and gastrointestinal cancer has been explained by differences in their biologic behavior. Nevertheless, controversy exists with respect to the appropriate treatment of regional lymph node metastases in gastrointestinal cancer. Some surgeons favor en bloc resection of the primary tumor and adjacent structures in combination with an extended lymph node dissection, while others argue that resection should be limited to the primary tumor and adjacent lymph nodes. The purpose of this review article is to evaluate the therapeutic efficacy of lymph node dissection in terms of survival of patients with gastrointestinal cancer.

ESOPHAGEAL CANCER

The lymphatic drainage of the esophagus is highly complex. Lymph nodes draining this region are widely distributed from the neck to the upper abdomen and demonstrate longitudinal lymphatic spread of esophageal cancer cells [14]. Esophagectomy, which consists of removing the muscular esophageal tube and any obviously enlarged lymph nodes through an abdominal and right chest approach [15], has been accepted as the gold standard for surgical management of esophageal cancer [16]. In recent years, more radical resection procedures such as posterior mediastinectomy [17], en bloc resection [18], and three-field dissection [19] have been developed in the hope of obtaining better local control and therefore improving the chance for cure. However, transhiatal esophagectomy has also been introduced [20,21] because of the potential for reduction in morbidity and mortality by avoiding thoracotomy [22,23], and it is the most common operation for esophageal cancer that does not include lymph node dissection. It has been criticized for denying an adequate esophageal resection and formal lymph node dissection to patients with potentially curable tumors [24,25].

It has been suggested that en bloc esophagectomy with

extended lymph node dissection provides better long-term survival than standard procedures [17,26–28]. In a retrospective comparative study, Skinner et al. [26] have reported that 1-year survival after en bloc resection (20/31, or 65%) was significantly greater ($P < .025$) than survival after standard resection (7/21, or 33%), the difference—55% vs. 14%, respectively ($P < .005$)—was even more apparent at 18 months (Table I). Similarly, Lerut et al. [28] have reported that extensive resection and extended lymphadenectomy significantly improved survival in patients undergoing an operation with curative intent. The 5-year survival was 48.5% vs. 41% for radical and nonradical resections, respectively ($P = .002$) (Table I). To our knowledge, however, there is no prospective randomized trial comparing en bloc esophagectomy with extended lymph node dissection to standard or conventional esophagectomy.

In the retrospective studies comparing transhiatal and transthoracic esophagectomy, Peracchia et al. [29], Tilanus et al. [30], Pac et al. [31], and Vigneswaran et al. [32] have reported that survival was not different between patients operated by the two approaches, while Fok et al. [33] did find a survival advantage for transthoracic esophagectomy (Table II). In prospective but nonrandomized studies, Hortsman et al. [34] and Shalian et al. [35] have failed to show that transthoracic esophagectomy with systemic two-field lymphadenectomy results in longer survival (Table II). Only one random-assignment study with a limited number of patients has been performed comparing transhiatal and transthoracic esophagectomy, both without any form of extended lymph node dissection. In this study, Goldminc et al. [36] found that overall survival in either node-negative or node-positive patients was not significantly different (Table II). However, transhiatal esophagectomy is not viewed as a procedure that is easier or safer than transthoracic esophagectomy, but rather as an alternative in the surgical armamentarium [35]. Transthoracic esophagectomy is preferred unless there are significant contraindications [33,37].

For carcinoma of the thoracic esophagus, en bloc esophagectomy with two-field lymphadenectomy is per-

TABLE II. Retrospective and Prospective Studies Comparing Transhiatal and Transthoracic Esophagectomy in Patients With Esophageal Cancer

Authors/ type of resection	No. of patients	Outcome		
Retrospective comparative study		5-Year survival rate		
Peracchia et al. [29]		<u>Metastases absent</u>	<u>Metastases present</u>	<u>Overall</u>
Transhiatal esophagectomy	140	28%] NS*
Transthoracic esophagectomy with standard lymphadenectomy	671	41%		
Pac et al. [31]		Overall 5-year survival rate		
Transhiatal esophagectomy	118	13%] NS*	
Transthoracic esophagectomy	120	10%		
Fok et al. [33]		Overall median survival time (months)		
Transhiatal esophagectomy	38	6.3] <i>P</i> = .048	
Transthoracic esophagectomy	172	11.3		
Prospective nonrandomized study				
Horstmann et al. [34]		Overall 3-year survival rate		
Transhiatal esophagectomy	46	21%] NS*	
Transthoracic esophagectomy	41	17%		
		Median survival time (months)		
Shalian et al. [35]		<u>Stage I</u>	<u>Stage III</u>	<u>Overall</u>
Transhiatal esophagectomy	30	23.1] NS*	14.1] NS*
Transthoracic esophagectomy	65	40.5		
Prospective randomized study		Overall survival		
Goldminc et al. [36]		<u>Metastases absent</u>	<u>Metastases present</u>	<u>Overall</u>
Transhiatal esophagectomy	32	NS*	NS*	NS*
Transthoracic esophagectomy	35			

*NS, P value is not significant.**TABLE III. Retrospective and Prospective Studies Comparing Two-Field and Three-Field Lymph Node Dissection in Patients With Esophageal Cancer**

Authors/type of resection	No. of patients	Outcome							
Retrospective comparative study		5-Year survival rate							
Akiyama et al. [39]		<u>Stage I</u>		<u>Stage IIA</u>		<u>Stage IIB</u>	<u>Stage III</u>	<u>Stage IV</u>	
3-field lymph node dissection	269	94%] NS*		83%] NS*		57%] NS*	56%] $P = .002$	28%] $P = .012$	
2-field lymph node dissection	272	69%]		48%]		47%]	27%]	11%]	
		<u>Metastases absent</u>				<u>Metastases present</u>		<u>Overall</u>	
3-field lymph node dissection	273	84%] $P = .0045$				43%] $P = .0008$		54%] $P = .0013$	
2-field lymph node dissection	290	55%]				28%]		38%]	
Isono et al. [40]		5-Year survival rate							
		<u>No metastases</u>		<u>Regional metastases</u>		<u>Distant metastases</u>	<u>Overall</u>		
3-field lymph node dissection	1,740	57%] $P < .01$		33%] $P < .05$		22%] $P < .05$	34%] $P < .001$		
2-field lymph node dissection	2,671	46%]		30%]		17%]	27%]		
Prospective randomized study		3-Year survival rate							
Kato et al. [41]		<u>Stage I</u>		<u>Stage IIA</u>		<u>Stage IIB</u>	<u>Stage III</u>	<u>Stage IV</u>	<u>Overall</u>
3-field lymph node dissection	77	46%] NS*		82%] NS*		71%] NS*	50%] $P < .05$	31%] $P < .01$	49%] $P < .01$
2-field lymph node dissection	73	75%]		15%]		100%]	27%]	0%]	34%]

*NS, P value is not significant.

TABLE IV. Retrospective Studies Comparing Conventional and Extended Lymph Node Dissection in Patients With Gastric Cancer†

Authors/type of resection	No. of patients	Outcome		
Mine et al. [48] and Majima et al. [49]	84	<u>Metastases absent</u>	5-Year survival rate	
		53%] NS*	<u>Metastases present</u>	<u>Overall</u>
		49%]	10%] NS*	
Inokuchi [50] and Kodama et al. [51]	254	<u>Metastases absent</u>	5-Year survival rate	
		73%] NS*	<u>Metastases present</u>	<u>Overall</u>
		81%]	18%] $P < .0001$	33%] $P < .0001$
Miwa et al. [52]	97	<u>Metastases absent</u>	10-Year survival rate	
		97%] NS*	<u>Metastases present</u>	<u>Overall</u>
		99%]	56%] $P < .018$	88%] $P < .005$

†DO, incomplete dissection of N1 lymph nodes; D1, complete dissection of N1 lymph nodes; D2, complete dissection of both N1 and N2 lymph nodes; D3, complete dissection of N1, N2, and N3 lymph nodes.

*NS, P value is not significant.

formed in Europe and North America [18,38], while cervicothoracoabdominal three-field dissection is preferred in Japan [39–41]. In a retrospective study, Akiyama et al. [39] compared 324 patients who underwent three-field lymphadenectomy and 393 who underwent two-field lymphadenectomy. The 5-year survival for Stage I to III patients was greater for the three-field lymphadenectomy group (Table III). These investigators have suggested that cervical lymph node metastases represent a regional and still controllable extent of disease [42]. However, such a difference could be attributed to inadequate staging with two-field dissection [43]. Nevertheless, in Stage IV disease with distant nodal metastases, three-field lymphadenectomy demonstrated a survival advantage with 28% of patients in this group living 5 years as compared to 11% of patients undergoing a standard dissection (Table III). In a Japanese nationwide collaborative study, Isono et al. [40] have analyzed whether there is prognostic benefit to three-field as compared to two-field lymphadenectomy. Cervical lymph node metastases were demonstrated in 27% of the patients treated with a three-field lymphadenectomy. In this study, they compared 1,740 patients who underwent three-field lymphadenectomy with 2,671 two-field lymphadenectomy patients. Overall, the three-field lymphadenectomy improved the 5-year survival rate as much as 7% as compared to two-field lymphadenectomy (Table III). A critical disadvantage of this study is the fact that it was a retrospective multicenter study. This study also lacked quality control regarding histologic examination of the resected esophagus and dissected lymph nodes [27]. Only one randomized study comparing three-field and two-field dissection has been performed. In this study, Kato et al. [41] found that three-field dissection offered a better 3-year survival rate than two-field dissection (49% vs. 34%, respectively; Table III). However, this study also has been criticized on the basis of selection bias

[29,43]. In the two-field lymphadenectomy group, there were older patients and more tumors located in the upper-midthoracic esophagus. There were also more T3 and T4 tumors in those undergoing two-field dissection. This results in selection of favorable cases for three-field lymphadenectomy, which probably influences survival rates. The concept of three-field lymph node dissection is still alien to most Western surgeons, and many would regard the presence of metastatic deposits in the cervical lymph nodes as distant metastases and evidence of incurability. Thereby, two opposite surgical attitudes exist at present. Some surgeons favor en bloc resection of the primary tumor and adjacent structures in combination with an extended dissection of the abdominal and mediastinal lymph nodes (“two-field”) and even including cervical lymph nodes (“three-field”) [18,26,39–41]. Others argue that resection should be limited to the primary tumor and adjacent lymph nodes [16,44].

GASTRIC CANCER

In the early 1960s, Jinnai et al. [45,46] recommended radical dissection of the lymph nodes to improve outcome in gastric cancer. Subsequently, the concept of radical dissection of lymph nodes has become an integral part of surgical treatment for this neoplasm in Japan. Gastric resection is classified according to the extent of the accompanying nodal dissection [47]. D0 represents gastric resection including incomplete dissection of the perigastric nodes (N1); D1 represents gastric resection including complete dissection of the N1 nodes; D2 is gastric resection including complete dissection of the N1 nodes and the nodes located along the splenic and left gastric arteries and the celiac axis (N2); and D3 is gastric resection including complete dissection of the N1 and N2 nodes and the nodes located along the hepatoduodenal ligament and at the root of the mesentery (N3). In a retrospective comparative study, Mine et al. [48] and

TABLE V. Prospective Nonrandomized Studies Comparing Conventional and Extended Lymph Node Dissection in Patients With Gastric Cancer†

Authors/ type of resection	No. of patients	Outcome					
		Stage I		Stage II		5-Year survival rate	
Pacelli et al. [53]						Stage IV	Overall
Limited lymph node dissection (D1)	121	82%	NS*	58%	NS*	30%	50%
Extensive lymph node dissection (D2-3)	117	86%		66%		49%	65%
						$P = .02$	$P = .01$
						—	
						5-Year survival rate	
Siewert et al. [54]		Stage IA		Stage IB		Stage II	Stage IIIA
Standard lymph node dissection (D1)	558	87%	NS*	72%	NS*	27%	25%
Complete or radical lymphadenectomy (D2)	1,096	86%		69%		55%	38%
							$P = .03$
							28%
							18%
							16%
							28%
							16%

†DO, incomplete dissection of N1 lymph nodes; D1, complete dissection of N1 lymph nodes; D2, complete dissection of both N1 and N2 lymph nodes; D3, complete dissection of N1, N2, and N3 lymph nodes.

*NS, P value is not significant.

Majima et al. [49] have reported that the 5-year survival rate was considerably higher after D3 resection than D2 resection (21% vs. 10%, respectively) in patients with positive lymph nodes, although this difference was not statistically significant (Table IV). In a similar patient population, Inokuchi [50] and Kodama et al. [51] have reported that the 5-year survival rate was significantly higher after D2 or D3 resection compared with D0 or D1 resection (39% vs. 18%, respectively, $P < .0001$, Table IV). In patients with early gastric cancer, Miwa et al. [52] have recently reported that the 10-year survival rate was significantly higher after D2 or D3 resection compared with D0 or D1 resection (98% vs. 88%, respectively, $P < .005$; Table IV). In a prospective, nonrandomized comparative study, Pacelli et al. [53] have shown that the 5-year survival rate was significantly higher after D2 or D3 compared with D1 resections (65% vs. 50%, respectively, $P = .01$; Table V). Similarly, Siewert et al. [54] have reported that the 5-year survival rate was significantly higher after D2 resection than after D1 resection in Stage II (55% vs. 27%, respectively, $P < .001$) and Stage IIIA patients (38% vs. 25%, respectively, $P = .03$; Table V). However, it has been suggested that such a large increase in survival cannot be explained by the performance of more radical lymphadenectomy [55–58]. Retrospective Japanese studies have been performed on groups of patients from two different periods of time, and therefore caution must be exercised in drawing conclusions from these studies. Moreover, the application of extended lymph node dissection results in substantial stage migration [59–61]. Recently, Bunt et al. [61] have calculated the effects of this stage migration on 5-year survival rates. Their data suggest an increase of 1% in tumor node metastasis Stage IA, 2% in IB, 7% in II, 15% in IIIA, and 15% in IIIB. Because of a lack of prospective

randomized studies, the improved results of extended lymph node dissection have not yet been substantiated [62]. No prospective study has been performed evaluating the efficacy of lymph node dissection in Japan. Such prospective randomized studies have been performed in Western countries [63–66] (Table V). However, Dent et al. [63] and Robertson et al. [64] in admittedly small studies have failed to demonstrate the efficacy of extended lymph node dissection (Table VI). Recently, Cuschieri et al. [65] have reported the preliminary results of a large randomized trial comparing D1 and D2 dissection. The survival at 3 years was 30% in patients whose gastrectomy included en bloc pancreatico-splenic resection vs. 50% in the remaining patients (Table VI). They have suggested that the higher mortality when the pancreas and spleen were resected nullifies any survival benefit from the D2 procedure. Nevertheless, the operative mortality rate associated with extended surgery in Japan is less than 3% [52,67,68], comparable with mortality rates for conventional resection in Western countries. Therefore, extended lymph node dissection remains the surgical procedure of choice for the curative treatment of most patients with gastric cancer in Japan [69]. However, we await the final results of the other prospective randomized clinical trials that involve a large number of patients [66].

COLORECTAL CANCER

The basic principle in the surgical management of colorectal cancer is en bloc resection of the primary tumor together with its vascular supply and the mesentery that contains the draining lymphatics. The lymph node dissection involves dissection in two directions—from the tumor central to the nodes along the course of the main arterial trunk and toward the epicolic and paracolic nodes

TABLE VI. Prospective Randomized Studies Comparing Limited and Extended Lymph Node Dissection in Patients With Gastric Cancer†

Authors/ type of resection	No. of patients	Outcome
Dent et al. [63]		No. of cancer-related death
Limited lymph node dissection (D1)	22	4
Extensive lymph node dissection (D2)	21	5
Robertson et al. [64]		Mean survival (days)
Limited lymph node dissection (D1)	25	1,511
Extensive lymph node dissection (D2)	29	922
Cuschieri et al. [65]		3-Year survival rate
Limited lymph node dissection (D1)	200	50%
Extensive lymph node dissection (D2)	200	30%

†D1, complete dissection of N1 lymph nodes; D2, complete dissection of both N1 and N2 lymph nodes.

*NS, *P* value is not significant.

located parallel to the intestine [70]. The extent of lymphatic resection with colonic or rectal cancer has long been controversial. The proximal site for transecting the bowel is determined by the level of ligation of the vascular pedicle. Limited vs. extended lymphatic dissection most often implies ligation of the vascular pedicle at a low vs. high level, respectively. A more aggressive approach has been advocated with high ligation of the inferior mesenteric artery and subsequently a more extended lymphadenectomy. Pezim and Nicholls [71] have compared 784 patients in whom the inferior mesenteric artery was ligated below the origin of the left colic artery (low ligation) with 586 in whom it was ligated above this level (high ligation). They found no difference in the 5-year survival for patients with Duke's A, B, or C1 tumors. In Duke's Stage C2, patients in the high ligation group fared significantly less well than similarly staged patients in the low ligation group (Table VII). Bacon and Khubchandani [72] have compared a series of patients who had undergone extensive retroperitoneal dissection and radical hemicolectomy with patients who had undergone only segmental resection. They found a 6% increase in 5-year survival in the group that underwent radical resection, although the difference was not statistically significant (Table VII). Rossi et al. [73] have compared the results of hemicolectomy with those of segmental resection. They found an increase in the 5-year survival rate from 54% to 66% with hemicolectomy, although this result was not statistically significant (Table VII). Thus, most retrospective studies investigating the value of extended resection or high ligation do not demonstrate a

significant benefit [71,74,75], although a difference has been suggested for sigmoid cancers [72,75,76].

Early in this century, Miles [77] advocated removal of the pelvic mesocolon in a combined abdominal and perineal approach for rectal cancer. Abdominopelvic lymph nodes were not usually removed by Miles abdominoperineal resection. Extended lymphadenectomy, involving dissection of pelvic and aortoiliac lymph nodes without resection of organs other than the rectum, has been practiced by Stearns and Deddish [78] and examined in a retrospective comparative study. The 5-year survival for the extended operation was 40% among Duke's C patients, while the 5-year survival for patients undergoing conventional resection was 23% (Table VIII). While these data were limited by small numbers and were not statistically significant, the suggestion of clinical superiority prompted others to examine the role of extended resections in rectal cancer. Enker et al. [79] have reported a large retrospective series consisting of 412 patients. One hundred ninety-two underwent en bloc aortoiliac pelvic lymphadenectomy (PLND), while 220 patients underwent more conservative or conventional resection. The PLND is not the same as the abdominopelvic lymphadenectomy reported by Stearns and Deddish [78]. This dissection includes the nodes caudad to the aortocaval bifurcation and along the common iliac arteries and veins and the internal iliac and middle hemorrhoidal branches of the pelvic blood supply. Anything less than a defined pelvic lymphadenectomy was considered a conventional resection. The overall 5-year survival of those patients undergoing pelvic lymph node dissection was 64%, which was significantly better than the survival of patients undergoing any lesser procedure (54%; *P* = .026). Although statistically significant enhancement of survival was not seen in Duke's A or B patients, this survival advantage for pelvic lymphadenectomy was observed in Duke's C patients (Table VIII). In Japan, Hojo et al. [80] have reported a series of 437 patients in whom 192 had wide PLND (extended excision). The cumulative 5-year survival rates in patients who underwent extended excision were 88% in Duke's B patients and 61% in Duke's C patients. In those who underwent conventional excision, survival rates were 74% in Duke's B patients and 43% in Duke's C patients. The differences between extended and conventional excision groups were statistically significant (*P* < 0.05; Table VIII). However, Glass et al. [81] have reported that patients who underwent abdominopelvic dissection at St. Mark's Hospital between 1960 and 1981 had a 5-year survival rate of 55%. This was similar to a previous series reported by Lockhart-Mummery et al. [82] for patients treated by conventional radical operation at the same hospital between 1948 and 1972 (57%; Table VIII). The St. Mark's experience suggests that an improvement in survival is unlikely to be achieved by extended resec-

TABLE VII. Retrospective Studies Comparing High and Low Ligation in Patients With Colorectal Cancer

Authors/type of resection	No. of patients	Outcome				
		5-Year survival rate				
Pezim and Nicholls [71]		<u>Duke's A</u>	<u>Duke's B</u>	<u>Duke's C1</u>	<u>Duke's C2</u>	<u>Overall</u>
Low ligation	784	81%] N*	65%] N*	43%] NS*	40%] <i>P</i> < .05]
High ligation	586	95%]	71%]	44%]	19%]	NS
		5-Year survival rate				
		Descending colon and sigmoid		Upper rectum	Lower rectum	Overall
Bacon et al. [72]		63%] NS*		52%] NS*	50%] NS*	55%] NS*
Low ligation	348	74%]		58%]	53%]	61%]
High ligation						
Rossi et al. [73]		Overall 5-Year survival rate				
Low ligation (segmental resection)	154	54%]	NS			
High ligation (hemicolectomy)	137	66%]				
		5-Year survival rate				
Surtees et al. [74]		<u>Astler-Coller C1</u>	<u>Astler-Coller C2</u>		<u>Duke's C1</u>	
Low ligation	100		80%] NS*	51%] NS*	54%] NS*	
High ligation	150		77%]	53%]	64%]	

*NS, P value is not significant.

TABLE VIII. Retrospective Studies Comparing Conventional and Extended Lymph Node Dissection in Patients With Rectal Cancer

Authors/type of resection	No. of patients	Outcome				
5-Year survival rate						
Stearns and Deddish [78]		<u>Duke's A</u>	<u>Duke's B</u>	<u>Duke's C</u>	<u>Overall</u>	
Resection without abdominopelvic lymph node dissection	442	72%] NS*	58%] NS*	23%] NS*	46%] NS*	
Resection plus abdominopelvic lymph node dissection	122	83%]	58%]	40%]	54%]	
5-Year survival rate						
Enker et al. [79]		<u>Duke's A</u>	<u>Duke's B</u>	<u>Duke's C</u>	<u>Overall</u>	
Conventional resection	220	84%] NS*	62%] NS*	29%] $P = .03$	54%] $P = .026$	
En bloc or extended lymphadenectomy	192	85%]	53%]	48%]	64%]	
5-Year survival rate						
Hojo et al. [80]		<u>Duke's A</u>	<u>Duke's B</u>	<u>Duke's C</u>		
Conventional lymphadenectomy	245	91%] NS*	74%] $P < .05$	43%] $P < .05$		
Extended lymphadenectomy	192	94%]	88%]	61%]		
5-Year survival rate						
Glass et al. [81] and Lockhart-Mummery et al. [82]		<u>Duke's A</u>	<u>Duke's B</u>	<u>Duke's C1</u>	<u>Duke's C2</u>	<u>Overall</u>
Conventional lymphadenectomy	55	82%] NS*	66%] NS*	40%] NS*	22%] NS*	57%] NS*
Extended lymphadenectomy	2,266	100%]	78%]	29%]	25%]	55%]

*NS, P value is not significant.

tions. The claimed superiority of extended lymphadenectomy is mainly based on retrospective studies [13]. However, it is difficult to interpret the retrospective results since the additional medical attention given in trials may prolong survival [83]. It is not yet clear whether extended resections do, in fact, increase survival in patients with colorectal cancer [84].

COMMENT

Most studies claiming the survival advantage of extended lymph node dissection in the treatment of gastro-

intestinal cancer are based on retrospective or nonrandomized studies. These studies are difficult to interpret since personal and special care given in trials may prolong survival. Although several randomized clinical trials have been performed for gastric cancer, they have failed to demonstrate the therapeutic benefit of extended lymph node dissection. It may be that the higher mortality nullifies the benefit of extended lymph node dissection. However, there are few well-done prospective randomized trials that directly address the issue of lymph node control of cancer cell dissemination in esophageal or co-

lorectal cancer. Therefore, the therapeutic value of extended lymph node dissection remains to be determined. Some surgeons may have difficulty with the concept of randomization of patients when they believe one treatment may be superior to the other, even if that is based only on anecdotal evidence [85]. Within the bounds of the ethical treatment of patients, however, randomized prospective studies can and should be done [86], since different human cancers display remarkable variability in their biologic behavior.

Even if the survival advantage of extended lymph node dissection is not demonstrated, we should avoid therapeutic nihilism and follow a principle of practical radicalism that minimizes morbidity and mortality whenever possible. There is no doubt that more accurate staging can be achieved by extended lymph node dissection. It is highly probable that the incidence of local recurrence is reduced by extended lymph node dissection. Lymph node dissection remains a reliable method of assessing nodal status and providing regional control in gastrointestinal cancer as well as breast cancer. Although chemotherapy is of limited therapeutic value in gastrointestinal cancer at present, the effect of chemotherapy and host defenses may depend on reducing the tumor burden to below a certain critical mass. The value of systemic therapy in patients treated by extended lymph node dissection as compared to those with residual microscopic disease remains a question of significant interest.

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